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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/306,986	05/07/1999	THUAN QUOC TRINH	IVGN 202	4261

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EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
01/09/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/306,986	TRINH ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-13,56 and 70-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-13,56 and 70-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/14/2008 has been entered.

Applicant's amendment of claim 8, in the papers of 1/14/2008, 6/20/2008 and 10/6/2008 are acknowledged.

Claims 8-13, 56 and 70-75 remain at issue and are present for examination. Applicant's review of the case history of the present application is also acknowledged and appreciated. Applicants' arguments filed on 1/14/2008 and 5/1/2006, have been fully considered.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8-13, 56, 70-75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 (9-13, 56, 70-75 dependent upon) is indefinite in that the reference "mixing the crude preparation with one or more…" is unclear and confusing on a number of different bases.

First, there is no antecedent basis for "the crude preparation" as this reference to "the crude preparation", is the first such reference.

Second it is unclear as to whether the reference "with" is intended to characterize what is "mixed" or the preparation itself. In the first possible interpretation "with" is used to separate the two articles that are mixed (i.e. 1) the preparation and 2) the DNA polymerase and ribonuclease). In the second interpretation "with" is used to describe the preparation, such as what the preparation contains (i.e. the preparation contains a DNA polymerase and a ribonuclease). Each of these two different interpretations lead to differences in the interpretation of the claimed method steps and are thought to be appropriate.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 8-13, 56, 70-75 are rejected under 35 U.S.C. 102(b) as being anticipated by Major (Biotechniques 12:40-43, 1992) as evidenced by Deana and Belasco (Mol. Microbiology, Vol. 51, No. 4, pp 1205-1217, 2004) and O'Donnell (Journal of Biological Chemistry, Vol 262, No. 34, pp 16558-16565, 1987).

It is noted that while this is similar to that rejection previously maintained in the non-final office action mailed to applicants on 7/25/2008, this rejection is different from that rejection previously appealed on 10/24/2006.

Major teaches a rapid PCR method of screening for point mutations. The taught method involves ascertaining the presence of a desired mutation within the mutated fragment or within some vector into which the mutated fragment has been cloned. Major teaches a method which comprises the synthesis of a nucleic acid molecule from a preparation comprising RNA and double-stranded DNA, said method comprising mixing the preparation with one or more DNA polymerases and incubating said mixture under conditions sufficient to synthesize a nucleic acid molecule complementary to all or a portion of a template nucleic acid molecule. The method taught by Major specifically involves the PCR amplification, using Taq DNA polymerase, of a DNA fragment from the expression plasmid, pBluescript 11 SK(+), either sampled directly from JM109 *E. coli* colonies or from a bacterial plasmid isolate. Major further teaches that some primers, especially those with a 3'-terminal T-'T mismatch result in extra minor bands when bacterial colony lysates were used for the starting material. This thus decreases

the sensitivity of the taught assay. Major does not teach the inclusion of an exogenous ribonuclease in the taught method, however, the bacterial lysate mixture taught by Major inherently comprises a ribonuclease. The inherency of ribonuclease in the mixture and thus the method taught by Major is evidenced by Deana and Belasco (Mol. Microbiology, Vol 51 No. 4, pp 1205-1217, 2004) who teach that *E. coli* inherently comprise a number of RNases that are capable of degrading single stranded RNA. It is noted that the reference Deana and Belasco is not available as prior art, however, this is unnecessary as this reference is only used to evidence that which is inherent in that method taught by Major.

Additionally it is noted to applicants that *E. coli* inherently contains a number of DNA polymerases, as evidenced by O'Donnell, Journal of Biological Chemistry, Vol 262, No. 34, pp 16558-16565, 1987).

Major specifically teach on page 40, column 3, "One medium-size colony was subjected to vigorous vortexing..." thus meeting the limitation of mixing the crude preparation with one or more DNA polymerases and one or more peptides or polypeptides having ribonuclease activity (See above rejection and discussion under 112 second paragraph). Major further teach the subsequent incubation of said prepared bacterial lysate with a pcr buffer, nucleotides and primers, sufficient to synthesize a nucleic acid molecule complementary to a portion of a double stranded DNA.

It is noted that while Major do not necessarily teach that said methods include a detectably labeled nucleotide, claim 13 is drawn to the method of claim 10 which is

drawn to the inclusion of such detectably labeled nucleotide in the alternative. Further claims 70-75 are included in the rejection because claims 70-75 appear to specify the "conditions sufficient to synthesize " a specific type of double stranded DNA. As the "conditions sufficient to synthesize " taught by Major et al. are sufficient to synthesize each of the various double stranded DNAs recited in claims 70-75, these claims are included in the rejection.

Applicants traversal of the previous rejection of claims 8-12, 56 and 70-73 under 35 U.S.C. 102(b) as being anticipated by Major (Biotechniques 12:40-43, 1992) as evidenced by Deana and Belasco (Mol. Microbiology, Vol. 51, No. 4, pp 1205-1217, 2004) is acknowledged and is considered to the extent that it applies to the current now **different** rejection, as well as that rejection made under 112 second paragraph.

Much of applicants previous argument is based upon the submission that the "clarified bacterial colony lysate" used in the assay of Major does not necessarily contain RNAses. This line of argument is not found relevant to the current rejection which focuses on the "medium size colony" discussed above.

It continues that nothing in applicants claimed method excludes that the RNase or the DNA polymerase, cannot inherently be a part of the preparation comprising RNA and double-stranded DNA. There is no method step which requires that an RNase or the DNA polymerase, which is external to the preparation be added to the preparation.

Thus claims 8-13, 56, 70-75 are anticipated by Major as evidenced by Deana and Belasco and O'Donnell.

Claims 8-13, 56, 70-75 are rejected under 35 U.S.C. 102(b) as being anticipated by Maudru et al. (Journal of Virological Methods 66: 247-261, July 1997).

Maudru discloses the method of the claimed invention at page 250 beginning in the bottom of column 1 in the section entitled "2.2.2. *Polymerase chain reaction (PCR)".* This section describes conduction of PCR in the presence of both RNase and thermostable DNA polymerase. Thus Maudru describes a step of "a) mixing the preparation with one or more DNA polymerases, and one or more peptides or polypeptides having ribonuclease activity, wherein said peptides or polypeptides having ribonuclease activity are capable of degrading single-stranded RNA," as claimed. The preparation of Maudru et al. is considered a crude preparation as applicant's specification states that: "The composition is especially useful in DNA synthesis when the sample is crude, i.e. prepared rapidly such that it contains contaminating RNA". Because Maudru conducts PCR using a double stranded DNA, Maudru discloses a step of "b) incubating said mixture under conditions sufficient to synthesize a nucleic acid molecule complementary to all or a portion of said double-stranded DNA and under which said peptides or polypeptides having ribonuclease activity degrade said single-stranded RNA," as claimed. Maudru section 2.2.2. further describes conducting RNAse digestion for 30 minutes prior to conducting PCR for 35 cycles and the inclusion of buffers and nucleotides. This procedure is conducted to reduce background signals

caused by an intrinsic RNA-dependent DNA polymerase activity of the thermostable Taq DNA polymerase, the enzyme used in PCR. (Maudru, abstract.). It is noted that while Maudru et al. do not necessarily teach that said methods include a detectably labeled nucleotide, claim 13 is drawn to the method of claim 10 which is drawn to the inclusion of such detectably labeled nucleotide in the alternative. Further claims 70-75 are included in the rejection because claims 70-75 appear to specify the "conditions sufficient to synthesize " a specific type of double stranded DNA. As the "conditions sufficient to synthesize " taught by Maudru et al. are sufficient to synthesize each of the various double stranded DNAs recited in claims 70-75, these claims are included in the rejection.

Thus Maudru anticipates claim 8-13, 56, 70-75.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

rgh
1/5/2008

/Richard G Hutson/
Primary Examiner, Art Unit 1652